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☐ 1: Hum Gene Ther. 1998 Oct 10;9(15):2277-84.

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Ex vivo breast cancer cell purging by adenovirus-mediated cytosine deaminase gene transfer and short-term incubation with 5-fluorocytosine completely prevents tumor growth after transplantation.

Wolff G, Korner IJ, Schumacher A, Arnold W, Dorken B, Mapara MY.

Department of Hematology, Oncology, and Tumor Immunology, Robert-Rossle-Klinik, University Medical Center, Charite, Humboldt University of Berlin, Germany.

Peripheral blood progenitor harvests of breast cancer patients are contaminated with tumor cells, suggesting a potential role for these cells in the relapse after high-dose chemotherapy. Whereas physical purging methods do not eliminate contaminating tumor cells completely, pharmacological purging, although highly efficient, is hampered by a strong nonspecific toxicity toward hematopoietic progenitor cells. Taking advantage of the high efficiency of adenovirus-mediated gene transfer to epithelial cells, we selectively loaded breast cancer cells in vitro with a cytotoxic drug by gene transfer of the prodrug-converting enzyme cytosine deaminase (AdCMV.CD) and 5-fluorocytosine (5-FC). Despite the low dose of vector administered, limited exposure to 5-FC, and transplantation only of viable tumor cells into SCID mice, all animals that received cells treated in vitro with AdCMV.CD plus 5-FC were completely free of tumor development. These data show that the selective loading of tumor cells with AdCMV.CD/5-FC might be useful for purging of autografts.

PMID: 9794211 [PubMed - indexed for MEDLINE]

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=> oncolytic
L1 1815 ONCOLYTIC

=> VSV
L2 4830 VSV

=> L1 and L2
L3 48 L1 AND L2

=> vivo
L4 816052 VIVO

=> L4 and L3
L5 23 L4 AND L3

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=> oncolysis

L6 201 ONCOLYSIS

=> VSV

2422 VSV
21 VSVS

L7 2424 VSV
(VSV OR VSVS)

=> L6 and l7

L8 7 L6 AND L7

=> D L8 IBIB ABS 1-7

L8 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:241128 CAPLUS
DOCUMENT NUMBER: 142:423269
TITLE: Treatment of multi-focal colorectal carcinoma metastatic to the liver of immune-competent and syngeneic rats by hepatic artery infusion of oncolytic vesicular stomatitis virus
AUTHOR(S): Shinozaki, Katsunori; Ebert, Oliver; Woo, Savio L. C.
CORPORATE SOURCE: Department of Gene and Cell Medicine, Mount Sinai School of Medicine, New York, NY, 10029-6574, USA
SOURCE: International Journal of Cancer (2005), 114(4), 659-664
CODEN: IJCNW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Viruses that replicate selectively in cancer cells hold considerable promise as novel therapeutic agents for the treatment of malignancy. The authors report an orthotopic model of multifocal colorectal cancer (CRC) metastases in the livers of syngeneic and immune-competent rats, which permitted rigorous testing of oncolytic virus vectors as novel therapeutic agents through hepatic arterial infusion for efficacy and safety. Vesicular stomatitis virus (VSV) is a neg.-strand RNA virus with intrinsic oncolytic specificity due to attenuated antiviral responses in many tumors. After administration at the maximum tolerated dose, the recombinant VSV vector gained access to multifocal hepatic CRC lesions that led to tumor-selective viral replication and **oncolysis**. No relevant vector-associated toxicities were noted and in particular, no damage to the hepatic parenchyma was seen. Moreover, the survival rate of vector-treated rats was significantly improved over that of animals in the control treatment group ($p = 0.015$). Our results demonstrate that hepatic arterial administration of oncolytic VSV is both effective and safe in an immune-competent and syngeneic rat model of multifocal CRC liver metastasis, suggesting that it can be developed into an effective therapeutic modality in patients in the future.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:361377 CAPLUS
DOCUMENT NUMBER: 141:370294
TITLE: Vesicular stomatitis virus: re-inventing the bullet
AUTHOR(S): Lichty, Brian D.; Power, Anthony T.; Stojdl, David F.; Bell, John C.
CORPORATE SOURCE: Ottawa Regional Cancer Centre Research Laboratories, Ottawa, ON, K1H 1C4, Can.
SOURCE: Trends in Molecular Medicine (2004), 10(5), 210-216
CODEN: TMMRCY; ISSN: 1471-4914
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. As the understanding of the mol. aspects of human disease increases, it is becoming possible to create designer therapeutics that are exquisitely targeted and have greater efficacy and fewer side effects. One class of targeted biol. agents that has benefited from recent advances in mol. biol. is designer viruses. Vesicular stomatitis virus (VSV) is normally relatively innocuous but can be engineered to target cancer cells or to stimulate immunity against diseases such as AIDS or influenza. Strains of VSV that induce or direct the production of interferon are superior to wild-type strains of the virus for inducing **oncolysis**. These strains might also make better vaccine vectors. In this review, some of the features that make VSV an excellent platform for the development of a range of viral therapeutics are discussed.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:190744 CAPLUS

DOCUMENT NUMBER: 140:350159
 TITLE: **Oncolysis** of Multifocal Hepatocellular Carcinoma in the Rat Liver by Hepatic Artery Infusion of Vesicular Stomatitis Virus
 AUTHOR(S): Shinozaki, Katsunori; Ebert, Oliver; Kournioti, Chryssanthi; Tai, Yun-Sheng; Woo, Savio L. C.
 CORPORATE SOURCE: Carl C. Icahn Center for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, NY, 10029-6574, USA
 SOURCE: Molecular Therapy (2004), 9(3), 368-376
 CODEN: MTOHCK; ISSN: 1525-0016
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Hepatocellular carcinoma (HCC) is a lethal malignancy with poor prognosis and few effective treatments, as well as ever-increasing frequencies in the Western world. Viruses that replicate selectively in cancer cells hold considerable promise as novel therapeutic agents for the treatment of malignancy. Vesicular stomatitis virus (VSV) is a neg.-strand RNA virus with intrinsic oncolytic specificity due to significantly attenuated antiviral responses in many tumor cells. The aim of this study was to evaluate the potential of VSV, administered via the hepatic artery, as an effective and safe therapeutic agent for treating "multifocal" HCC in the rat liver. Recombinant VSV vector expressing β -galactosidase (rVSV- β -gal) was generated by reverse genetics and infused into the hepatic artery of Buffalo rats bearing orthotopically implanted multifocal HCC. Access by the virus to multifocal HCC lesions in the liver, as well as the kinetic profiles of intratumoral viral replication and spread, was established by X-gal staining of liver and tumor sections. Plaque assays were also performed to determine the infectious viral yields in tumor and normal liver tissues. Pharmacotoxicol. studies, including serum chemistries and proinflammatory cytokine production, as well as organ histopathol., were performed. Buffer- or vector-treated tumor-bearing rats were followed for survival and the results were analyzed by the Kaplan-Meier method and the log-rank test. Hepatic arterial infusion of rVSV- β -gal at the maximum tolerated dose in tumor-bearing rats resulted in efficient viral transduction of multifocal HCC lesions in their livers, tumor-selective viral replication, and extensive **oncolysis**. Importantly, no significant vector-associated toxicities were noted and, in particular, no damage to the hepatic parenchyma was seen. Finally, survival of vector-treated rats was substantially prolonged over that of animals in the control treatment group ($p < 0.028$). Thus, hepatic arterial administration of VSV is both effective and safe in an orthotopic animal model of multifocal HCC. The results suggest that oncolytic VSV can be developed into an effective and safe therapeutic modality for patients with multifocal HCC in the future.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:115829 CAPLUS
 DOCUMENT NUMBER: 140:179252
 TITLE: Defective translational control facilitates vesicular stomatitis virus **oncolysis**
 AUTHOR(S): Balachandran, Siddharth; Barber, Glen N.
 CORPORATE SOURCE: Department of Microbiology and Immunology and Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL, 33136, USA
 SOURCE: Cancer Cell (2004), 5(1), 51-65
 CODEN: CCAECI; ISSN: 1535-6108
 PUBLISHER: Cell Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Vesicular stomatitis virus (VSV) exerts potent antitumor activity, although the mol. mechanisms underlying its oncolytic properties remain to be fully clarified. Here, we demonstrate that normally resistant murine embryonic fibroblasts are rendered highly permissive to VSV replication following cellular transformation, a progression

that appears to compromise the antiviral effects of interferon (IFN). Subsequent studies revealed normal dsRNA-dependent protein kinase (PKR) activation and phosphorylation of eukaryotic initiation factor 2 (eIF2) α . Nevertheless, eIF2B-mediated guanine nucleotide exchange activity downstream of eIF2 was frequently aberrant in transformed cells, neutralizing eIF2 α phosphorylation and permitting VSV mRNA translation. Thus, defects in translational regulation can cooperate with impaired IFN signaling to facilitate VSV replication, and may represent a common hallmark of tumorigenesis.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:982369 CAPLUS

DOCUMENT NUMBER: 140:58249

TITLE: The Oncolytic Effect of Recombinant Vesicular Stomatitis Virus Is Enhanced by Expression of the Fusion Cytosine Deaminase/Uracil Phosphoribosyltransferase Suicide Gene

AUTHOR(S): Porosnicu, Mercedes; Mian, Abdul; Barber, Glen N.

CORPORATE SOURCE: Department of Microbiology and Immunology and Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL, USA

SOURCE: Cancer Research (2003), 63(23), 8366-8376
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vesicular stomatitis virus (VSV) has recently been demonstrated to exhibit significant oncolytic capabilities against a wide variety of tumor models in vitro and in vivo. To potentially enhance the oncolytic effect, we generated a novel recombinant VSV (rVSV) that expressed the fusion suicide gene Escherichia coli cytosine deaminase (CD)/uracil phosphoribosyltransferase (UPRT). RSVS encoding the CD/UPRT fusion gene (VSV-C:U) exhibited normal growth properties and generated high levels of biol. active CD/UPRT that could catalyze the modification of 5-fluorocytosine into chemotherapeutic 5-fluorouracil (5-FU), which exhibited considerable bystander effect. Intratumoral inoculation of VSV-C:U in the presence of the systemically administered prodrug 5-fluorocytosine produced statistically significant redns. in the malignant growth of syngeneic lymphoma (A20) or mammary carcinoma (TSA) in BALB/c mice compared with rVSV treatments or with control 5-FU alone. Aside from detecting prolonged therapeutic levels of 5-FU in VSV-C:U-treated animals harboring TSA tumors and enhancing bystander killing of tumor cells, we demonstrated marked activation of IFN- γ -secreting cytotoxic T cells by enzyme-linked immunospot anal. that may have also facilitated tumor killing. In conclusion, the insertion of the fusion CD/UPRT suicide gene potentiates the oncolytic efficiency of VSV by generating a strong bystander effect and by contributing to the activation of the immune system against the tumor without detrimentally altering the kinetics of virus-mediated oncolysis and may be useful in the treatment of malignant disease.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:873978 CAPLUS

DOCUMENT NUMBER: 140:121916

TITLE: Vesicular stomatitis virus: An exciting new therapeutic oncolytic virus candidate for cancer or just another chapter from Field's virology?

AUTHOR(S): Giedlin, Martin A.; Cook, David N.; Dubensky, Thomas W., Jr.

CORPORATE SOURCE: Cancer Research, Cerus Corporation, Concord, CA, 94520, USA

SOURCE: Cancer Cell (2003), 4(4), 241-243
CODEN: CCAECI; ISSN: 1535-6108

PUBLISHER: Cell Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Selected mutant strains of vesicular stomatitis virus (VSV) are described that are unable to combat endogenous IFN- β signaling within infected normal cells and as a result are dramatically more selective for productive growth in tumor cells having a defective antiviral response. The VSV mutants may have the potential to be used clin. as a systemic oncolytic agent for the treatment of distal and metastatic cancers.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:668101 CAPLUS

DOCUMENT NUMBER: 140:104590

TITLE: Oncolysis of hepatic metastasis of colorectal cancer by recombinant vesicular stomatitis virus in immune-competent mice

AUTHOR(S): Huang, Tian-Gui; Ebert, Oliver; Shinozaki, Katsunori; Garcia-Sastre, Adolfo; Woo, Savio L. C.

CORPORATE SOURCE: Carl C. Icahn Center for Gene Therapy and Molecular Medicine, Mount Sinai School of Medicine, New York, NY, 10029-6574, USA

SOURCE: Molecular Therapy (2003), 8(3), 434-440

CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB With currently available treatments, patients with metastatic colorectal cancer (CRC) have a median survival of 14.8 mo and a 5-yr survival rate of less than 10%. In recent years, tumor-targeted replicating viruses have rapidly emerged as potential novel oncolytic agents for cancer treatment. Vesicular stomatitis virus (VSV) is a neg.-strand RNA virus with inherent selectivity for replication in tumor cells due to their attenuated antiviral response. VSV is particularly appealing as an oncolytic agent for its exceptionally rapid replication cycle in tumor cells, whereby it is capable of manifesting its maximal oncolytic effects before the onset of neutralizing antiviral immune responses in the host. In this study, we used a recombinant VSV vector expressing the green fluorescent protein gene (rVSV-GFP) to monitor VSV replication easily in CRC cells. Using this GFP-expressing virus, we found that rVSV-GFP efficiently replicated and lysed murine and human CRC cell lines in vitro. We also evaluated the potential of rVSV-GFP to treat MCA26 CRC metastases implanted orthotopically into the livers of syngeneic BALB/c mice. We provide conclusive evidence that rVSV-GFP is able to replicate extensively in the tumors, but not in normal liver cells, in tumor-bearing mice. A single intratumoral injection also caused extensive tumor necrosis, which led to a significant prolongation of animal survival. Our results indicate that VSV can be an effective and safe oncolytic agent against hepatic CRC metastasis in immune-competent mice and may be developed for the treatment of cancer patients in the future.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> VSV

L2 4830 VSV

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L3 48 L1 AND L2

=> vivo

L4 816052 VIVO

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L5 23 L4 AND L3

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L23 NOT FOUND

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L4 ANSWER 1 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1023425 CAPLUS
TITLE: The gene or medicine introduction revelation method of using the photoirradiation [Machine Translation].
INVENTOR(S): Shintome, Yasuo; Takahashi, Hironobu; Horiguchi, Yukichi; Shintome, Takuro; Nakajima, Kanako; Yamada, Atsushi
PATENT ASSIGNEE(S): Japan Science and Technology Agency, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005255582	A2	20050922	JP 2004-67306	20040310

PRIORITY APPLN. INFO.: JP 2004-67306 20040310

AB [Machine Translation of Descriptors]. The medicine substance, the functional mol. like the physiol. active material, or the gene and nuclear acid is introduced into in **vivo**, the technol. which reveals the function effectively is offered thing Effectively revelation and/or to promote revelation it is possible the function of the said functional mol. absorbing the pulse electromagnetic wave (light), the particle from fragmentation or from the substance which causes the fusion of the aggregate it forms, by irradiating the pulse electromagnetic wave which consists of the pulse electromagnetic wave in the said nano- particle which is introduced into in **vivo** in the in **vivo** introduction revelation method of the functional mol. which reveals the function of the functional mol. which functional mol. and compound material of the nano- particle is formed into in **vivo** the functional mol. carrier which -, to introduce to in **vivo**, it introduces, the nano- particle. Absorbing the pulsed radiation, the high-mol. nano- particle, micelle, the semiconductor nano- particle or the metal nano- particle which include the pigment, and/or it can list the aggregate of 1 type or plural types of these nano- particles as the nano- particle which consists of the substance which causes the fragmentation of the particle or the fusion of the aggregate.

L4 ANSWER 2 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1023283 CAPLUS
TITLE: Boron transporter - and its gene [Machine Translation].
INVENTOR(S): Fujiwara, Toru; Miwa, Kyoko
PATENT ASSIGNEE(S): Japan Science and Technology Agency, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005253430	A2	20050922	JP 2004-73338	20040315
PRIORITY APPLN. INFO.:			JP 2004-73338	20040315

AB [Machine Translation of Descriptors]. The transporter where it becomes possible, is known so far to control the transport of the boron with the taking in and in *vivo* of the boron from in environment more efficiently, - with offer the new gene which administers the boron transport which has the activity which differs. You acquired the complete length ccDna of 5 genes of At3g62270, At3g06450, At1g15460, At1g74810 and At5g25430 which have been revealed among the BOR1 homologous genes which exist in , in 5' with 3'; you constructed constructing which connected ccDna of the ORF part which excludes the side both non translation territory to GAL1 promoter downstream concerning these genes, introduced into yeast. When 60 min it cultured with the nutrient medium which includes boron, in each case you could see the decrease of fungus body inland water soluble boron d. by comparison with vector control.

L4 ANSWER 3 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:1023196 CAPLUS
 TITLE: Cosmetic preparation containing C24-fatty acids
 INVENTOR(S): Schreiner, Volker; Lanzendoerfer, Ghita; Bleckmann, Andreas; Raschke, Thomas; Kolbe, Ludger
 PATENT ASSIGNEE(S): Beiersdorf AG, Germany
 SOURCE: Ger. Offen., 29 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102004010246	A1	20050922	DE 2004-102004010246	20040302
PRIORITY APPLN. INFO.:			DE 2004-102004010246	20040302

AB [Machine Translation of Descriptors]. The present invention concerns cosmetic and dermatol. prepn. with a portion of C24-Fettsaeuren. The formulations according to invention contain good dermal availabilities of the long-chain C24-Fettsaeuren, which redultieren in improved in *vivo* effectivenesses. The cosmetic and/or dermatol. preparation on emulsion basis and/or hydro dispersion gels covers one or more fatty acids with a number of carbon from 22 to 28, with a portion to one or more C24-Fettsaeuren of over 30 weight percents, related to the total mass at fatty acids, and one or more medium/means-polar lipids with an interfacial surface tension against water between 20 and 30 mN/m.

L4 ANSWER 4 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:1023164 CAPLUS
 TITLE: Translational study of vitamin D differentiation therapy of myeloid leukemia: effects of the combination with a p38 MAPK inhibitor and an antioxidant
 AUTHOR(S): Wang, Q.; Harrison, J. S.; Uskokovic, M.; Kutner, A.; Studzinski, G. P.
 CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, UMDNJ-New Jersey Medical School, Newark, NJ, USA
 SOURCE: Leukemia (2005), 19(10), 1812-1817
 CODEN: LEUKED; ISSN: 0887-6924
 PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Human myeloid leukemia cell lines are induced to terminal differentiation into monocyte lineage by 1,25-dihydroxyvitamin D3 (1,25D3) or its analogs (deltanoids). However, translation of these findings to the clinic is limited by calcemic effects of deltanoids. Strategies to overcome this problem include combination of deltanoids with other compds. to induce differentiation at lower, noncalcemic, deltanoid concns. We previously showed that either carnosic acid, an antioxidant, or SB202190, a p38 MAPK inhibitor, increase the potency of 1,25D3 in the HL60 cell line. Here, we

report that simultaneous addition of both these agents further increases differentiation potency of deltanoids in this cell line and in freshly obtained leukemic cells *ex vivo*. Activity of MAPK pathways showed that increased differentiation was associated with enhanced activity of JNK pathway in all responding cell subtypes. Our studies suggest that patients with CML or AML subtypes M2 and M4, but not M1, M3 or M4eo, are particularly suitable for this combination therapy. We conclude that the established cell line HL60 presents a good model for some, but not all, subtypes of myeloid leukemia, and that the JNK pathway plays an important role in monocytic differentiation of human leukemic cells *ex vivo*, as well as *in vitro*. Leukemia (2005) 19, 1812-1817.

L4 ANSWER 5 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1023151 CAPLUS
TITLE: Compensatory PI3-kinase/Akt/mTor activation regulates imatinib resistance development
AUTHOR(S): Burchert, A.; Wang, Y.; Cai, D.; von Bubnoff, N.; Paschka, P.; Mueller-Bruesselbach, S.; Ottmann, O. G.; Duyster, J.; Hochhaus, A.; Neubauer, A.
CORPORATE SOURCE: Klinik fuer Haematologie, Klinikum der Philipps Universitaet Marburg, Onkologie und Immunologie, Marburg, Germany
SOURCE: Leukemia (2005), 19(10), 1774-1782
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB BCR/ABL-kinase mutations frequently mediate clin. resistance to the selective tyrosine kinase inhibitor Imatinib mesylate (IM, Gleevec). However, mechanisms that promote survival of BCR/ABL-pos. cells before clin. overt IM resistance occurs have poorly been defined so far. Here, we demonstrate that IM-treatment activated the phosphatidylinositol 3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTor)-pathway in BCR/ABL-pos. LAMA-cells and primary leukemia cells *in vitro*, as well as in a chronic phase CML patient *in vivo*. In fact, PI3K/Akt-activation critically mediated survival during the early phase of IM resistance development before manifestation of BCR/ABL-dependent strong IM resistance such as through a kinase mutation. Accordingly, inhibition of IM-induced Akt activation using mTor inhibitors and Akt-specific siRNA effectively antagonized development of incipient IM-resistance *in vitro*. In contrast, IM-resistant chronic myeloid leukemia (CML) patients with BCR/ABL kinase mutations (n=15), and IM-refractory BCR/ABL-pos. acute lymphatic leukemia patients (n=2) displayed inconsistent and kinase mutation-independent autonomous patterns of Akt-pathway activation, and mTor-inhibition overcame IM resistance only if Akt was strongly activated. Together, an IM-induced compensatory Akt/mTor activation may represent a novel mechanism for the persistence of BCR/ABL-pos. cells in IM-treated patients. Treatment with mTor inhibitors may thus be particularly effective in IM-sensitive patients, whereas Akt-pathway activation variably contributes to clin. overt IM resistance. Leukemia (2005) 19, 1774-1782.

L4 ANSWER 6 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1023127 CAPLUS
TITLE: Developmental competence and gene expression in preimplantation bovine embryos derived from somatic cell nuclear transfer using different donor cells
AUTHOR(S): Jang, Goo; Jeon, Hyun Yong; Ko, Kyung Hee; Park, Hee Jung; Kang, Sung Keun; Lee, Byeong Chun; Hwang, Woo Suk
CORPORATE SOURCE: Department of Theriogenology and Biotechnology, College of Veterinary Medicine, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Zygote (2005), 13(3), 187-195
CODEN: ZYGOEB; ISSN: 0967-1994
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study compared the developmental competence of somatic cell nuclear

transfer (SCNT) embryos reconstructed with different donor cells and analyzed gene expression in the resulting embryos. Bovine fetal/adult ear fibroblasts and cumulus cells were used as donor cells and the developmental competence of the reconstructed embryos was monitored. The cell number and allocation in blastocysts were determined by differential staining. The Bax, E-cad, IF-tau, Hsp (heat shock protein) 70, Igf2r (insulin-like growth factor 2 receptor), DNMT (DNA methyltransferase) 1 and Mash (mammalian achaete-scute homolog) 2 genes were selected for gene expression anal. The relative abundance (ratio to GAPDH mRNA) of gene transcripts in blastocysts was measured by semiquant. reverse transcription-polymerase chain reaction. In experiment 1, development of SCNT preimplantation embryos and the cell nos. of inner cell masses and trophoblasts were not different among SCNT embryos derived from different cell types. In experiment 2, the relative expression of GAPDH and Hsp 70 transcripts was similar in all embryos. The expression of Bax, Igf2r and Mash2 transcripts was significantly increased in SCNT embryos reconstructed with adult fibroblasts. The E-cad transcript levels were reduced in SCNT embryos reconstructed with fetal fibroblasts. Relative abundance of DNMT1 in SCNT embryos derived from fetal fibroblasts was increased, and IF-tau expression in SCNT embryos derived from cumulus cells was increased. In conclusion, depending on the type of donor cells, preimplantation SCNT embryos displayed marked differences in gene expression. This may affect the developmental competence of SCNT embryos reconstructed with different cell types after implantation or during fetal growth in *vivo*.

L4 ANSWER 7 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:1023025 CAPLUS
 TITLE: Comparative toxic potency ranking of chlorophenols
 AUTHOR(S): Pepelko, William E.; Gaylor, David W.; Mukerjee, Debdas
 CORPORATE SOURCE: Sciences International, Inc., Alexandria, VA, 22314, USA
 SOURCE: Toxicology and Industrial Health (2005), 21(5-6), 93-111
 CODEN: TIHEEC; ISSN: 0748-2337
 PUBLISHER: Arnold, Hodder Headline
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Chlorophenols are prevalent in all media of the environment. The most common environmental source of pentachlorophenol (PCP) and other chlorinated phenols are via the lumber industry as a wood preservative and as a pesticide in plant production. The US Environmental Protection Agency's (EPA) contaminant candidate list (CCL) includes a majority of these compds. as unregulated contaminants. Except for pentachlorophenol, there is a lack of human or animal data base which can be used for human health risk assessment. The specific aim of this study is to develop a rationale to use in *vivo* nonmammalian, in vitro mammalian and nonmammalian, micro-organism toxicity data base, structural activity, mechanistic and toxicokinetic data bases for developing a relative toxic potency ranking scheme of chlorophenols. Although the toxic potency of chlorophenols was found to increase with the number of chlorines, the potency decreases if the chlorines are attached in the ortho position of the mols. Based on the LOAELs and mammalian in vitro data, the relative potency of chlorophenols determined to be best estimated by the ratios of log Kow to the 0.55 power. The relationship of the toxic potency derived from such an approach is largely presumptive.

L4 ANSWER 8 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:1022938 CAPLUS
 TITLE: Integrin-linked kinase in renal disease: Connecting cell - matrix interaction to the cytoskeleton
 AUTHOR(S): Blattner, Simone Monika; Kretzler, Matthias
 CORPORATE SOURCE: Nephrology Center, University of Munich, Munich, Germany
 SOURCE: Current Opinion in Nephrology & Hypertension (2005), 14(4), 404-410
 CODEN: CNHYEM; ISSN: 1062-4821
 PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Integrin-linked kinase has emerged as a key player at the interface between extracellular matrix, integrins, actin-based cytoskeleton and cellular phenotype in kidney diseases. Future studies focusing on interacting mols. and modification of integrin-linked kinase function in **vivo** will better define the role of cell matrix signalling in progressive renal failure.

L4 ANSWER 9 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022877 CAPLUS
TITLE: Changes in basal cell mitosis and transepidermal water loss in skin cultures treated with vitamins C and E
AUTHOR(S): Parish, W. E.; Read, J.; Paterson, S. E.
CORPORATE SOURCE: Unilever Corporate Research, Colworth, Sharnbrook, Bedford, UK
SOURCE: Experimental Dermatology (2005), 14(9), 684-691
CODEN: EXDEEY; ISSN: 0906-6705
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three variants of the living skin equivalent cultures were compared in order to determine the most suitable to grow human differentiated epidermis to test beneficial properties of nutrients. Criteria of culture quality were mitotic index and transepidermal water loss (TEWL) assayed by means of a ServoMed Evaporimeter EP-2TM (ServoMed, Kinna, Sweden). Stds. were donor skin mean mitotic index 11.1% and TEWL of living subjects mean 6.4 g/m²/h. Cultures (i) in 5% serum, 10 ng/mL of epidermal growth factor (EGF) at 37°C and 95% relative humidity (RH); mitotic index on day 14, 19.2%, but on day 21, 1.8% and TEWL 9.5 g/m²/h on day 18. (ii) In 1% serum, no EGF, 33°C and 95% RH, mitotic index on day 21, 9.1% and TEWL, 9.5% on day 18. (iii) Culture in same medium, 33°C and 60% RH, mitotic index on day 28, 9.5% and TEWL 6.1 g/m²/h on day 18 as in **vivo**. Incubation in 60% RH was achieved using a novel chamber and dishes exposing only the corneum, sealing the medium. Vitamins C and E were used as model test nutrients. Culture conditions were 1% serum, no EGF at 33°C and 95% RH. Vitamin C at 142 and 284 µM increased the mitotic index after 10- and 15-day treatment, but at 586 µM it was weakly toxic. Vitamin E at 20 and 40 µM did not. Both vitamins reduced TEWL providing functional data in support of previous reports on barrier properties. These are functional biomarkers of skin benefit relevant to skin in **vivo**.

L4 ANSWER 10 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022874 CAPLUS
TITLE: Experimental approaches to lymphocyte migration in dermatology in vitro and in **vivo**
AUTHOR(S): Radeke, Heinfried H.; Ludwig, Ralf J.; Boehncke, Wolf-Henning
CORPORATE SOURCE: Pharmazentrum Frankfurt, Dr-Hans-Schleussner-Foundation Immune Pharmacology, Frankfurt, Germany
SOURCE: Experimental Dermatology (2005), 14(9), 641-666
CODEN: EXDEEY; ISSN: 0906-6705
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lymphocyte trafficking through the dermal compartment is part of the physiol. surveillance process of the adaptive immune system. On the other hand, persistent or recurrent lymphocyte infiltrates are hallmarks of both types of chronic inflammatory skin diseases, Th1-type such as psoriasis or Th2/allergic-type like atopic dermatitis. A better understanding of the mechanisms underlying lymphocyte movements is one of the key prerequisites for developing more effective therapies. In this review, we introduce a range of simple-to-sophisticated exptl. in vitro and in **vivo** approaches to analyze lymphocyte migration. These methods start from static in vitro adhesion and chemotaxis assays, include dynamic endothelial flow chamber, intravital dual photon, and transcutaneous live-video microscopy, and finally encompass specific genetically deficient or engineered animal models. Discussing pros and cons of these

assay systems hopefully generates both state-of-the-art knowledge about the factors involved in most common chronic skin diseases as well as an improved understanding of the limitations and chances of new biol. pharmaceuticals that are currently introduced into clin. practice.

L4 ANSWER 11 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022866 CAPLUS
TITLE: Darunavir
AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bayes, M.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2005), 30(5), 441-449
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human immunodeficiency virus type 1 (HIV-1) infection remains a major global health problem due to the emergence of drug-resistant strains. Thus, there is an ongoing need for new therapeutics for the long-term management of HIV infection and for acute HIV-1 infection due to drug-resistant strains. HIV-1 protease inhibitors (PIs) have proven to be effective addns. to existing antiretroviral regimens. However, despite the success of these agents, the emergence of mutants conferring multidrug resistance (MDR) remains a critical problem. Darunavir is a next-generation nonpeptide PI that exhibits potent antiviral activity with low toxicity in vitro and in vivo. The agent retains activity against resistant strains and has a low liability for the development of resistance. Darunavir is entering phase III clin. trials and has shown excellent promise as a treatment for HIV-1 infection in treatment-experienced patients.

L4 ANSWER 12 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022845 CAPLUS
TITLE: The effects of thermochemotherapy using cyclophosphamide plus hyperthermia on the malignant pleural mesothelioma in vivo
AUTHOR(S): Riehemann, Kathrin; Schmitt, Oliver; Ehlers, Eva-Maria
CORPORATE SOURCE: Institut fuer Anatomie, Universitaet zu Luebeck, Luebeck, 23538, Germany
SOURCE: Annals of Anatomy (2005), 187(3), 215-223
CODEN: ANANEY; ISSN: 0940-9602
PUBLISHER: Elsevier GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human malignant pleural mesothelioma is related to the use of asbestos in the majority of cases. Though the use of asbestos has been prohibited since the 1990s, the incidence of pleural mesothelioma is still increasing because of a latency period of at least 20 years. This study investigated the benefit of single therapy with cyclophosphamide or hyperthermia or the combination of both on cells of a human pleural mesothelioma cell line, xenotransplanted s.c. in the paw of mice. A CONTROL group received the same volume of physiol. saline. The oxygenation of tumors was measured, tumor growth was followed over 3 wk, immunohistochem. studies and a light and electron microscopic evaluation were performed. Chemotherapy or hyperthermia alone was only temporarily effective. The greatest benefit was achieved using combined thermochemotherapy consisting of cyclophosphamide plus hyperthermia: 50% of this group had partial remissions, and 67% responded to this therapy. After 3 wk tumors grew again. Superior effects could be achieved by performing addnl. cycles of chemotherapy or adding another drug or radiation for instance. This study shows promising results in the treatment of malignant pleural mesothelioma.

L4 ANSWER 13 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022669 CAPLUS
TITLE: Ethanol breaks dormancy of the potato tuber apical bud
AUTHOR(S): Claassens, Margo M. J.; Verhees, John; van der Plas, Linus H. W.; van der Krol, Alexander R.; Vreugdenhil, Dick
CORPORATE SOURCE: Laboratory of Plant Physiology, WUR, Wageningen

SOURCE: University, Wageningen, 6703 BD, Neth.
Journal of Experimental Botany (2005), 56(419),
2515-2525
CODEN: JEBOA6; ISSN: 0022-0957
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Growing potato tubers or freshly harvested mature tubers have a dormant apical bud. Normally, this dormancy is spontaneously broken after a period of maturation of the tuber, resulting in the growth of a new sprout. Here it is shown that in *in vitro*-cultured growing and maturing tubers, ethanol can rapidly break this dormancy and re-induce growth of the apical bud. The *in vivo* promoter activity of selected genes during this secondary growth of the apical bud was monitored, using luciferase as a reporter. In response to ethanol, the expression of carbohydrate-storage, protein-storage, and cell division-related genes are rapidly down-regulated in tuber tissue. It was shown that dormancy was broken by primary but not by secondary alcs., and the effect of ethanol on sprouting and gene expression in tuber tissue was blocked by an inhibitor of alc. dehydrogenase. By contrast, products derived from alc. dehydrogenase activity (acetaldehyde and acetic acid) did not induce sprouting, nor did they affect luciferase reporter gene activity in the tuber tissue. Application of an inhibitor of gibberellin biosynthesis had no effect on ethanol-induced sprouting. It is suggested that ethanol-induced sprouting may be related to an alc. dehydrogenase-mediated increase in the catabolic redox charge [NADH/(NADH+NAD⁺)].

L4 ANSWER 14 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022653 CAPLUS
TITLE: A variety of synergistic and antagonistic interactions mediated by cis-acting DNA motifs regulate gene expression in plant cells and modulate stability of the transcription complex formed on a basal promoter
AUTHOR(S): Sawant, Samir V.; Kiran, Kanti; Mehrotra, Rajesh; Chaturvedi, Chandra Prakash; Ansari, Suraiya A.; Singh, Pratibha; Lodhi, Niraj; Tuli, Rakesh
CORPORATE SOURCE: National Botanical Research Institute, Lucknow, 226001, India
SOURCE: Journal of Experimental Botany (2005), 56(419), 2345-2353
CODEN: JEBOA6; ISSN: 0022-0957
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several synthetic promoters containing a variety of commonly found cis-acting DNA sequence motifs were constructed to study the motif-motif and motif-protein interactions involved in gene expression in plants. Transient expression of the reporter gene gusA in tobacco leaves was used to demonstrate that several sequence elements can be arranged upstream of a basal promoter to function synergistically in enhancing gene expression. A cis-acting DNA motif could function as an activator by itself as well as a synergizing activator in the presence of other homologous as well as heterologous motifs in the neighborhood. The function of a complex promoter comprising several activation motifs was arrested nearly completely in *in vivo*, following titration with any one of the motifs. The results suggested a hierarchical assembly of several motif-binding factors, leading to the stabilization of the transcriptional complex formed on the TATA-box.

L4 ANSWER 15 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022648 CAPLUS
TITLE: Plant cell signaling: In *in vivo* and -omics approaches
AUTHOR(S): Pandey, Sona; Perfus-Barbeoch, Laetitia; Taylor, J. Philip; Zhao, Zhixin
CORPORATE SOURCE: 208 Mueller Lab, Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Journal of Plant Growth Regulation (2005), 24(1), 46-54

PUBLISHER: Springer Science+Business Media, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Unavailable

L4 ANSWER 16 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022560 CAPLUS
TITLE: Suppression of metastasis of human pancreatic cancer to the liver by transportal injection of recombinant adenoviral NK4 in nude mice
AUTHOR(S): Murakami, Mitsuhiko; Nagai, Eishi; Mizumoto, Kazuhiro; Saimura, Michiyo; Ohuchida, Kenoki; Inadome, Naoki; Matsumoto, Kunio; Nakamura, Toshikazu; Maemondo, Makoto; Nukiwa, Toshihiro; Tanaka, Masao
CORPORATE SOURCE: Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
SOURCE: International Journal of Cancer (2005), 117(1), 160-165
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NK4, a 4-kringle fragment of hepatocyte growth factor (HGF), is an HGF antagonist that also acts as an angiogenesis inhibitor. NK4 strongly inhibits the infiltration, metastasis, and tumor growth of pancreatic cancer. The aim of our study was to evaluate the antitumor effect of adenovirus-mediated NK4 gene transfer to the liver on hepatic metastasis of pancreatic cancer in *vivo*. We constructed recombinant adenoviral NK4 (Ad-NK4), which encodes a secreted form of human NK4. Intrasplesenic injection of Ad-NK4 induced high and relatively maintained expression of NK4 protein in the liver and suppressed the number and growth of metastatic foci in the liver in a nude mouse model. Microscopically, central necrosis was found even in small metastatic foci in Ad-NK4 treated mice. Immunohistochem. anal. of metastatic tumors showed a remarkable decrease in microvessel d. and an increase in the number of apoptotic tumor cells after treatment with Ad-NK4. These results indicate that intraportal injection of Ad-NK4 may be a useful therapeutic modality for the clin. control of hepatic metastasis in pancreatic cancer.

L4 ANSWER 17 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022554 CAPLUS
TITLE: Switch of HLA-G alternative splicing in a melanoma cell line causes loss of HLA-G1 expression and sensitivity to NK lysis
AUTHOR(S): Rouas-Freiss, Nathalie; Bruel, Sylvie; Menier, Catherine; Marcou, Celine; Moreau, Philippe; Carosella, Edgardo D.
CORPORATE SOURCE: Service de Recherches en Hemato-Immunologie, CEA-DSV-DRM, Hopital Saint-Louis, IUH, Paris, Fr.
SOURCE: International Journal of Cancer (2005), 117(1), 114-122
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Considerable information has been accumulated on HLA-G expression in tumor lesions in which HLA-G is viewed as a way to turn off anti-tumoral immunity. Nevertheless, there is little data concerning the mechanisms by which expression and function of HLA-G are regulated in malignant cells. Here, we have addressed these points by studying a melanoma cell line derived from a surgically-removed HLA-G-pos. melanoma lesion. We show that HLA-G expression in melanoma cells can be regulated at the mRNA splicing level. Indeed, melanoma cells rapidly switched from cell-surface HLA-G1 to intra-cellular HLA-G2 expression. This mechanism restored tumor sensitivity to NK lysis. Moreover, switch from HLA-G1 to HLA-G2 was strong enough to prevent re-expression of immunoprotective HLA-G1 even following treatments with cytokines and DNA demethylating agent. Modulating HLA-G at the mRNA splicing level would be an efficient way of

lifting in **vivo** HLA-G-mediated tumor immune escape.

L4 ANSWER 18 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:1022548 CAPLUS

TITLE: Cyclosporine A and its non-immunosuppressive derivative NIM811 induce apoptosis of malignant melanoma cells in in vitro and in **vivo** studies

AUTHOR(S): Ciechomska, Iwona; Legat, Magdalena; Golab, Jakub; Wesolowska, Aleksandra; Kurzaj, Zuzanna; Mackiewicz, Andrzej; Kaminska, Bozena

CORPORATE SOURCE: Laboratory of Transcription Regulation, Department of Cell Biology, Nencki Institute of Experimental Biology, Warsaw, Pol.

SOURCE: International Journal of Cancer (2005), 117(1), 59-67
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Advanced melanoma is a highly malignant tumor with an increasing incidence that has a poor prognosis due to resistance to common therapeutic strategies. We have demonstrated previously that cyclosporine A (CsA) induces apoptosis of rat glioma cells, reactive astrocytes, and fibroblasts. In our present study, we investigated effects of CsA and its nonimmunosuppressive derivative NIM811 on survival of human and murine melanoma cells. We demonstrated that CsA and NIM811 affect survival of human and murine melanoma cells and induce morphol. changes, alterations in nuclear morphol. and an internucleosomal DNA fragmentation, consistent with an apoptotic type of death. Western blot anal. showed an activation of caspases 9, 7, 3 and PARP cleavage detectable at 24 h after exposure of human melanoma cells to the drugs. CsA and NIM811 induced a significant increase in subG1 population of murine B16F10 melanoma cells indicative of apoptotic DNA fragmentation. Studies in murine model of melanoma showed that NIM811, but not CsA, retards tumor progression and significantly decreases tumor volume after intratumoral application. Our findings indicate that CsA and its derivs. may be new candidates for the treatment of melanoma patients.

L4 ANSWER 19 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:1022547 CAPLUS

TITLE: Periostin is down-regulated in high grade human bladder cancers and suppresses in vitro cell invasiveness and in **vivo** metastasis of cancer cells

AUTHOR(S): Kim, Chul Jang; Yoshioka, Naohisa; Tambe, Yukihiro; Kushima, Ryoji; Okada, Yusaku; Inoue, Hirokazu

CORPORATE SOURCE: Department of Urology, Shiga University of Medical Science, Otsu, Shiga, Japan

SOURCE: International Journal of Cancer (2005), 117(1), 51-58
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have previously reported that expression of periostin mRNA is markedly reduced in a variety of human cancer cell lines, suggesting that downregulation of periostin mRNA expression is correlated with the development of human cancers. In our study, to clarify the role of the periostin in human bladder carcinogenesis, we examined the expression of periostin mRNA in normal bladder tissues, bladder cancer tissues and bladder cancer cell lines by Northern blot anal. and RT-PCR anal. Although the expression of periostin mRNA was detected in 100% (5/5) of normal bladder tissues, it was not detected in 3 human bladder cancer cell lines examined. It was also detected in 81.8% (9/11) of grade 1, 40.0% (4/10) of grade 2 and 33.3% (4/12) of grade 3 bladder cancer tissues, indicating that downregulation of periostin mRNA is significantly related to higher grade bladder cancer ($p < 0.05$). To assess the tumor suppressor function of periostin, we investigated the ability of periostin gene to suppress malignant phenotypes of a bladder cancer cell line, SBT31A. Ectopic expression of periostin gene by a retrovirus vector suppressed in

vitro cell invasiveness of the bladder cancer cells without affecting cell proliferation and tumor growth in nude mice. Periostin also suppressed in **vivo** lung metastasis of the mouse melanoma cell line, B16-F10. Mutational anal. revealed that the C-terminal region of periostin was sufficient to suppress cell invasiveness and metastasis of the cancer cells. Periostin may play a role as a suppressor of invasion and metastasis in the progression of human bladder cancers.

L4 ANSWER 20 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022546 CAPLUS
TITLE: Downregulation of laminin α 4 chain expression inhibits glioma invasion in vitro and in **vivo**
AUTHOR(S): Nagato, Shigeyuki; Nakagawa, Kou; Harada, Hironobu; Kohno, Shohei; Fujiwara, Hironobu; Sekiguchi, Kiyotoshi; Ohue, Shiro; Iwata, Shinji; Ohnishi, Takanori
CORPORATE SOURCE: Department of Neurosurgery, Ehime University School of Medicine, Ehime, Japan
SOURCE: International Journal of Cancer (2005), 117(1), 41-50
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The laminin family is a structural constituent of the extracellular matrix that plays an essential role in promoting the motility of infiltrative tumor cells. We investigated the role of laminin α 4 chain, a subset of laminin-8, -9 and -14, in the motile and invasive activities of human glioma cells. All malignant glioma cell lines examined expressed more mRNA for the laminin α 4 and β 1 chains than for the β 2 chain, indicating that these cells predominantly express the laminin-8 isoform. Introducing an antisense oligonucleotide for laminin α 4 chain (AS-Ln- α 4) into the glioma cells resulted in downregulation of laminin α 4 expression. AS-Ln- α 4 also significantly suppressed glioma cell adhesion and migration. Furthermore, invasiveness was significantly reduced in cells transfected with AS-Ln- α 4 compared to those transfected with the sense oligonucleotide (S-Ln- α 4). Indeed, when glioma spheroids were implanted into rat brain slices, AS-Ln- α 4-transfected cells failed to invade surrounding normal brain tissues. In addition, intracerebral injection of glioma cells transfected with AS-Ln- α 4 into nude mice resulted in the formation of a noninvasive tumor, whereas injection of cells transfected with S-Ln- α 4 resulted in diffuse invasion of brain tissue. These results suggest that mainly laminin-8 is essential for the invasive activity of human glioma cells; thus, a novel therapeutic strategy could target this mol. to treat patients with malignant glioma.

L4 ANSWER 21 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1022542 CAPLUS
TITLE: Expression of cytochromes P450 and glutathione S-transferases in human prostate, and the potential for activation of heterocyclic amine carcinogens via acetyl-CoA-, PAPS- and ATP-dependent pathways
AUTHOR(S): Di Paolo, Oscar A.; Teitel, Candee H.; Nowell, Susan; Coles, Brian F.; Kadlubar, Fred F.
CORPORATE SOURCE: Division of Pharmacogenomics and Molecular Epidemiology, National Center for Toxicological Research, Jefferson, AR, USA
SOURCE: International Journal of Cancer (2005), 117(1), 8-13
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dietary factors appear to be involved in the high incidence of prostate cancer in "Westernized" countries, implicating dietary carcinogens such as heterocyclic amines (HAs) in the initiation of prostate carcinogenesis. We examined 24 human prostate samples with respect to their potential for activation and detoxification of HAs and the presence of DNA adducts formed in **vivo**. Cytochromes P 450 1B1, 3A4 and 3A5 were expressed at low levels (<0.1-6.2 pmol/mg microsomal protein).

N-Acetyltransferase (NAT) activities, using p-aminobenzoic acid (NAT1) and sulfamethazine (NAT2) as substrates, were <5-5,500 and <5-43 pmol/min/mg cytosolic protein, resp. Glutathione S-transferases (GSTs) P1, M2 and M3 were expressed at 0.038-1.284, 0.005-0.126 and 0.010-0.270 µg/mg cytosolic protein, resp.; GSTM1 was expressed in all GSTM1-pos. samples (0.012-0.291 µg/mg cytosolic protein); and GSTA1 was expressed at low levels (<0.01-0.11 µg/mg cytosolic protein). Binding of N-hydroxy-PhIP to DNA in vitro occurred primarily by an AcCoA-dependent process (<1-54 pmol/mg/DNA), PAPS- and ATP-dependent binding being <1-7 pmol/mg DNA. In **vivo**, putative PhIP- or 4-aminobiphenyl-DNA adducts were found in 4 samples (0.4-0.8 adducts/108 bases); putative hydrophobic adducts were found in 6 samples (8-64 adducts/108 bases). Thus, the prostate appears to have low potential for N-hydroxylation of HAs but greater potential for activation of N-hydroxy HAs to genotoxic N-acetoxy esters. The prostate has potential for GSTP1-dependent detoxification of ATP-activated N-hydroxy-PhIP but little potential for detoxification of N-acetoxy-PhIP by GSTA1. However, there were no significant correlations between expression/activities and DNA adducts formed in vitro or in **vivo**, DNA adducts in **vivo** possibly reflecting carcinogen exposure.

L4 ANSWER 22 OF 816052 CAPLUS COPYRIGHT 2005, ACS on STN
 ACCESSION NUMBER: 2005:1022529 CAPLUS
 TITLE: Dynamic study of calcium phosphate formation on porous HA/TCP ceramics
 AUTHOR(S): Duan, Y. R.; Zhang, Z. R.; Wang, C. Y.; Chen, J. Y.; Zhang, X. D.
 CORPORATE SOURCE: State Key Laboratory for Modification of Chemical Fibers and Polymer Material, Donghua University, Shanghai, 200051, Peop. Rep. China
 SOURCE: Journal of Materials Science: Materials in Medicine (2005), 16(9), 795-801
 CODEN: JSMMEJ; ISSN: 0957-4530
 PUBLISHER: Springer
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Bone-like apatite formation on porous calcium phosphate ceramics was investigated in static simulated body fluid (SBF) and dynamic SBF at different flowing rates. The results of a 14-day immersion in static SBF showed that the formation of bone-like apatite occurred both on the surface and in the pores of the samples. When SBF flowed at the physiol. flow rate in muscle (2 mL/100 mL·min), bone-like apatite could be detected only in internal surface of the pores of samples. The result that bone-like apatite formation could only be found in the pores when SBF flowed at physiol. flow rate was consistent with that of porous calcium phosphate ceramics implanted in **vivo**: osteoinduction was only detected inside the pores of the porous calcium phosphate ceramics. This result implicates that the bone-like apatite may play an important role in the osteoinduction of Ca-P materials. The dynamic model used in this study may be better than usually used static immersion model in imitating the physiol. condition of bone-like apatite formation. Dynamic SBF method is very useful to understand bone-like apatite formation in **vivo** and the mechanism of ectopic bone formation in calcium phosphate ceramics.

L4 ANSWER 23 OF 816052 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2005:1022430 CAPLUS
 TITLE: Interaction of Pasteurella multocida with free-living amoebae
 AUTHOR(S): Hundt, Matthew J.; Ruffolo, Carmel G.
 CORPORATE SOURCE: Department of Biological Sciences, University of Wisconsin-Parkside, Kenosha, WI, USA
 SOURCE: Applied and Environmental Microbiology (2005), 71(9), 5458-5464
 CODEN: AEMIDF; ISSN: 0099-2240
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Pasteurella multocida is a highly infectious, facultative intracellular bacterium which causes fowl cholera in birds. This study reports, for the first time, the observed interaction between P. multocida and free-living

amoebae. Amoebal trophozoites were coinfectd with fowl-cholera-causing *P. multocida* strain X-73 that expressed the green fluorescent protein (GFP). Using confocal fluorescence microscopy, GFP expressing X-73 was located within the trophozoite. Transmission electron microscopy of coinfection prepns. revealed clusters of intact X-73 cells in membrane-bound vacuoles within the trophozoite cytoplasm. A coinfection assay employing gentamicin to kill extracellular bacteria was used to assess the survival and replication of *P. multocida* within amoebae. In the presence of amoebae, the number of recoverable intracellular X-73 cells increased over a 24-h period; in contrast, X-73 cultured alone in assay medium showed a consistent decline in growth. Cytotoxicity assays and microscopy showed that X-73 was able to lyse and exit the amoebal cells approx. 18 h after coinfection. The observed interaction between *P. multocida* and amoebae can be considered as an infective process as the bacterium was able to invade, survive, replicate, and lyse the amoebal host. This raises the possibility that similar interactions occur *in vivo* between *P. multocida* and host cells. Free-living amoebae are ubiquitous within water and soil environments, and *P. multocida* has been observed to survive within these same ecosystems. Thus, our findings suggest that the interaction between *P. multocida* and amoebae may occur within the natural environment.

ACCESSION NUMBER: 2000:428788 BIOSIS
DOCUMENT NUMBER: PREV200000428788
TITLE: Exploiting tumor-specific defects in the interferon pathway
with a previously unknown **oncolytic** virus.
AUTHOR(S): Stojdl, David F.; Lichty, Brian; Knowles, Shane; Marius,
Ricardo; Atkins, Harold; Sonenberg, Nahum; Bell, John C.
[Reprint author]
CORPORATE SOURCE: Ottawa Regional Cancer Centre Research Laboratories, 501,
Smyth Road, Ottawa, ON, K1H 8L6, Canada
SOURCE: Nature Medicine, (July, 2000) Vol. 6, No. 7, pp. 821-825.
print.
ISSN: 1078-8956.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Interferons are circulating factors that bind to cell surface receptors,
activating a signaling cascade, ultimately leading to both an antiviral
response and an induction of growth inhibitory and/or apoptotic signals in
normal and tumor cells. Attempts to exploit the ability of interferons to
limit the growth of tumors in patients has met with limited results
because of cancer-specific mutations of gene products in the interferon
pathway. Although interferon-non-responsive cancer cells may have
acquired a growth/survival advantage over their normal counterparts, they
may have simultaneously compromised their antiviral response. To test
this, we used vesicular stomatitis virus (**VSV**), an enveloped,
negative-sense RNA virus exquisitely sensitive to treatment with
interferon. **VSV** rapidly replicated in and selectively killed a
variety of human tumor cell lines even in the presence of doses of
interferon that completely protected normal human primary cell cultures.
A single intratumoral injection of **VSV** was effective in reducing
the tumor burden of nude mice bearing subcutaneous human melanoma
xenografts. Our results support the use of **VSV** as a
replication-competent **oncolytic** virus and demonstrate a new
strategy for the treatment of interferon non-responsive tumors.

ACCESSION NUMBER: 2001:242607 BIOSIS

DOCUMENT NUMBER: PREV200100242607

TITLE: **Oncolytic** activity of vesicular stomatitis virus
is effective against tumors exhibiting aberrant p53, ras,
or myc function and involves the induction of apoptosis.

AUTHOR(S): Balachandran, Siddharth; Porosnicu, Mercedes; Barber, Glen
N. [Reprint author]

CORPORATE SOURCE: University of Miami School of Medicine, 1550 NW 10th Ave.,
Rm. 514, Papanicolaou Building, M710, Miami, FL, 33136, USA
gbarber@med.miami.edu

SOURCE: Journal of Virology, (April, 2001) Vol. 75, No. 7, pp.
3474-3479. print.
CODEN: JOVIAM. ISSN: 0022-538X.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 16 May 2001

Last Updated on STN: 19 Feb 2002

AB. We have recently shown that vesicular stomatitis virus (**VSV**)
exhibits potent **oncolytic** activity both in vitro and in vivo (S.
Balachandran and G. N. Barber, IUBMB Life 50:135-138, 2000). In this
study, we further demonstrated, in vivo, the efficacy of **VSV**
antitumor action by showing that tumors that are defective in p53 function
or transformed with myc or activated ras are also susceptible to viral
cytolysis. The mechanism of viral **oncolytic** activity involved
the induction of multiple caspase-dependent apoptotic pathways was
effective in the absence of any significant cytotoxic T-lymphocyte
response, and occurred despite normal PKR activity and eIF2alpha
phosphorylation. In addition, **VSV** caused significant inhibition
of tumor growth when administered intravenously in immunocompetent hosts.
Our data indicate that **VSV** shows significant promise as an
effective **oncolytic** agent against a wide variety of malignant
diseases that harbor a diversity of genetic defects

ACCESSION NUMBER: 2001:53684 BIOSIS
DOCUMENT NUMBER: PREV200100053684
TITLE: Vesicular stomatitis virus (VSV) therapy of
tumors.
AUTHOR(S): Balachandran, Siddharth; Barber, Glen N. [Reprint author]
CORPORATE SOURCE: University of Miami School of Medicine, 1550 NW 10th Ave.,
514 Papanicolaou Bldg., Miami, FL, 33136, USA
gbarber@med.miami.edu
SOURCE: IUBMB Life, (August, 2000) Vol. 50, No. 2, pp. 135-138.
print.
ISSN: 1521-6543.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002

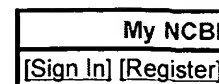
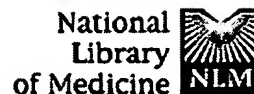
AB Vesicular stomatitis virus (VSV) is an essentially nonpathogenic
negative-stranded RNA virus, the replication of which is extremely
sensitive to the antiviral effects of interferon (IFN). We demonstrate
here that VSV selectively induces the cytolysis of numerous
transformed human cell lines in vitro, with all the morphological
characteristics of apoptotic cell death. Importantly, VSV can
also potently inhibit the growth of p53-null C6 glioblastoma tumors in
vivo without infecting and replicating in normal tissue. With our
previous findings demonstrating that primary cells containing the
double-stranded RNA-activated protein kinase PKR and a functional IFN
system are not permissive to VSV replication, these results
suggest that signaling by IFN may be defective in many malignancies. Thus
VSV might be useful in novel therapeutic strategies for targeting
neoplastic disease.

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#1	Search oncolytic and ex vivo Field: All Fields, Limits: Publication Date to 2000/06/26	12:15:42	2
#38	Search ex vivo purging and oncolytic virus Limits: Publication Date to 2000/06/26	12:12:19	4
#33	Search ex vivo purging and transplantation and cancer therapy Limits: Publication Date to 2000/06/26	12:10:18	150
#30	Search ex vivo purging and transplantation and oncolytic virus Limits: Publication Date to 2000/06/26	12:08:42	3
#29	Search ex vivo purging and transplantation Limits: Publication Date to 2000/06/26	12:08:32	210
#22	Search ex vivo and advantage and purging Limits: Publication Date to 2000/06/26	12:02:08	6
#21	Search ex vivo and advantage Limits: Publication Date to 2000/06/26	12:01:49	93
#19	Related Articles for PubMed (Select 14248702)	12:00:58	101
#14	Search oncolytic and transplantation and leukemia Limits: Publication Date to 2000/06/26	11:59:05	9
#6	Search oncolytic and transplantation Limits: Publication Date to 2000/06/26	11:57:03	51
#10	Search oncolytic and auto transplantation and Limits: Publication Date to 2000/06/26	11:56:45	0
#9	Search oncolytic and autotransplantation and Limits: Publication Date to 2000/06/26	11:56:38	0
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ACCESSION NUMBER: 2004:725783 CAPLUS

TITLE: Vesicular Stomatitis Virus: A Potential Therapeutic Virus for the Treatment of Hematologic Malignancy

AUTHOR(S): Lichty, Brian D.; Stojdl, David F.; Taylor, Rebecca A.; Miller, Leigh; Frenkel, Irina; Atkins, Harold; Bell, John C.

CORPORATE SOURCE: Ottawa Regional Cancer Centre Research Laboratories, Ottawa, ON, K1H 1C4, Can.

SOURCE: Human Gene Therapy (2004), 15(9), 821-831
CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Certain strains of vesicular stomatitis virus (VSV) have been shown to be **oncolytic** in a wide variety of solid tumors. In the present study, we tested the leukemolytic properties of VSV using established leukemia cell lines and primary patient material. VSV efficiently killed essentially all leukemic cell lines. In contrast, however, normal clonogenic bone marrow progenitor cells and peripheral blood cells were remarkably refractory to infection by VSV. By exploiting this large difference in susceptibility to infection we successfully purged contaminating leukemic cells from cultures of peripheral blood progenitor cells (PBPC) using VSV. VSV was also able to infect and kill leukemic cells in primary samples taken from patients with multiple myeloma (MM). This study demonstrates the potential utility of VSV in the treatment, both **ex vivo** and **in vivo**, of hematol. malignancies.

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ACCESSION NUMBER: 2004:423955 BIOSIS

DOCUMENT NUMBER: PREV200400419862

TITLE: Vesicular stomatitis virus: A potential therapeutic virus for the treatment of hematologic malignancy.

AUTHOR(S): Lichty, Brian D.; Stojdl, David F.; Taylor, Rebecca A.; Miller, Leigh; Frenkel, Irina; Atkins, Harold; Bell, John C. [Reprint Author]

CORPORATE SOURCE: Res Labs, Ottawa Reg Canc Ctr, 503 Smyth Rd, Ottawa, ON, K1H 1C4, Canada
jbell@ohri.ca

SOURCE: Human Gene Therapy, (September 2004) Vol. 15, No. 9, pp. 821-831. print.
ISSN: 1043-0342 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Nov 2004

Last Updated on STN: 3 Nov 2004

AB Certain strains of vesicular stomatitis virus (VSV) have been shown to be **oncolytic** in a wide variety of solid tumors. In the present study, we tested the leukemolytic properties of VSV using established leukemia cell lines and primary patient material. VSV efficiently killed essentially all leukemic cell lines. In contrast, however, normal clonogenic bone marrow progenitor cells and peripheral blood cells were remarkably refractory to infection by VSV. By exploiting this large difference in susceptibility to infection we successfully purged contaminating leukemic cells from cultures of peripheral blood progenitor cells (PBPC) using VSV.

VSV was also able to infect and kill leukemic cells in primary samples taken from patients with multiple myeloma (MM). This study demonstrates the potential utility of VSV in the treatment, both *ex vivo* and *in vivo*, of hematologic malignancies.

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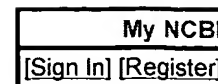
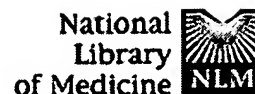
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1: J Hematother. 1997 Oct;6(5):441-6.

Related Articles, Links

Ex vivo treatment of bone marrow with phosphorothioate oligonucleotide OL(1)p53 for autologous transplantation in acute myelogenous leukemia and myelodysplastic syndrome.**Bishop MR, Jackson JD, Tarantolo SR, O'Kane-Murphy B, Iversen PL, Bayever E, Joshi SM, Sharp JG, Pierson JL, Warkentin PI, Armitage JO, Kessinger A.**

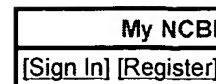
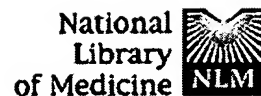
Department of Internal Medicine, University of Nebraska Medical Center, Omaha 68198-3330, USA.

Effective ex vivo purging techniques can decrease the likelihood of infusing bone marrow contaminated with leukemic cells during autologous transplantation. In preliminary studies, OL(1)p53, a 20-mer phosphorothioate oligonucleotide directed against p53 mRNA, decreased the number of acute myelogenous leukemia (AML) cells in vitro, suggesting a possible role for OL(1)p53 in purging bone marrow harvests of leukemia cells. To demonstrate that OL(1)p53 was nontoxic to hematopoietic progenitor cells, normal bone marrow cells were incubated with 10 microM OL(1)p53 for 36 h, and hematopoietic progenitor cell survival was determined by in vitro colony assays. OL(1)p53 had no toxic effect on the growth of either myeloid (CFU-GM) or erythroid (BFU-E) progenitor cells. OL(1)p53 was then used to ex vivo purge bone marrow harvests from nine patients with either AML or myelodysplastic syndrome (MDS). Bone marrow cells were incubated with 10 microM OL(1)p53 for 36 h before transplantation. The median times posttransplantation for the patient to recover an absolute neutrophil count greater than $0.5 \times 10^9/L$ and a platelet transfusion independence were 30 days and 56 days, respectively. Incubation of bone marrow cells with OL(1)p53 had no detrimental effect on the growth of hematopoietic progenitor cells, and transplantation of autologous bone marrow cells treated with the phosphorothioate oligonucleotide, OL(1)p53, resulted in successful recovery of circulating neutrophils following high-dose therapy in patients with AML or MDS. The data show that OL(1)p53 can be used safely to purge autologous bone marrow harvests from patients with leukemia.

Publication Types:

- Clinical Trial

PMID: 9368180 [PubMed - indexed for MEDLINE]



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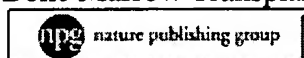
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☐ 1: Bone Marrow Transplant. 1999 Sep;24(6):621-7.

Related Articles, Links

**Autologous bone marrow transplantation for high risk acute lymphoblastic leukemia: clinical relevance of ex vivo bone marrow purging with monoclonal antibodies and complement.****Granena A, Castellsague X, Badell I, Ferrer C, Ortega J, Brunet S, Puntí C, Sureda A, Picon M, Valls A, Rutllant M, Garcia J.**

Hematology Department, 'Institut Catala d'Oncologia', Barcelona, Spain.

Herein we describe our experience with 75 consecutive autologous BM transplants for patients with high-risk ALL, with special attention to the clinical impact of BM purging. Fifty-two patients received purged BM using monoclonal antibody (MoAb) cocktails and complement, and 23 patients received untreated BM. The distribution of prognostic factors was similar in both groups. Hemopoietic reconstitution was adequate and did not differ in the two groups. Transplant-related mortality was 9.6% and 13% in 'purged' and 'unpurged' groups. Median follow up was 11 months (2-71) and overall actuarial probability of disease-free survival (DFS) at 5 years was 40% (53% relapse probability). We found a beneficial effect of purging in patients over 15 years of age and in patients needing more than 1 month to reach CR1. Patients in CR1 receiving purged marrow had a longer DFS and a lower relapse probability (52% vs 12%, $P = 0.02$ and 35% vs 86%, $P = 0.005$, respectively) which were related to the efficacy of the purging procedure (more or less than one log of depletion). In further CR, no advantage of purging has been found. Our data strongly suggest the clinical relevance of BM purging in autologous BMT in high-risk ALL patients and support the need for prospective randomized studies.

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